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13. ABSTRACT (Maximum 200 words) The purpose of the IDEA award is to establish a cohort of 50,000 vigorous exercisers, provide data on questionnaire validity and provide pilot data on surveillance. (Funding for surveillance will be deferred to a future funding application.) During this first year of funding, we finalized the design of the survey questionnaire and obtained approval from human subjects for its use, determined the best recruitment strategy for recruiting 50,000 women runners, obtained the names of over one-half million women runners, delivered the questionnaire to be printed and collated, arranged for their mailing, and designed the system for archiving the surveys as they are received. We had originally intended to create the cohort of 50,000 runners by combining our original cohort of 14,000 women runners collected between 1991 and 1996 with surveys from an additional 36,000 women runners recruited through the current grant. However, the consent for human subjects obtained for the initial 14,000 women runners is inconsistent with the Department of Defense human use protocol, hence we will create a de novo sample of 50,000 women runners. We expect to obtain all 50,000 questionnaires by the end of January, 1999.				
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FOREWORD

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Introduction Epidemiological studies suggest that regular exercise may reduce breast cancer risk. One hypothesis for this finding is that breast cancer risk increases with the cumulative number of ovulatory cycles. Strenuous physical exercise may reduce breast cancer risk by reducing the frequency of ovulatory cycles through delayed menarche, luteal suppression, oligomenorrhea, amenorrhea and/or accelerated menopause. To date, there have been no prospective studies of the association between strenuous physical activity and breast cancer.

Women who were athletically active in college are reported to have decreased breast cancer risk [1; 2]. Frish et al studied 2622 former college athletes and 2776 non-athletes [2]. The age-adjusted rates for breast cancer were 10.1/1000 for athletes and 15.6/1000 for nonathletes [2]. Bernstein et al [3] conducted personal interviews with a total of 545 women (aged 40 and younger at diagnosis) who had been newly diagnosed with in situ or invasive breast cancer and 545 control subjects in a case control study. After adjustment for potential confounding factors, they found that the average number of hours spent in physical exercise activities per week from menarche to 1 year prior to the case patient's diagnosis significantly predicted reduced breast cancer risk ($P < .0001$ for trend). The odds ratio (OR) of breast cancer among women who, on average, spent 3.8 or more hours per week participating in physical exercise activities, was 0.42 (95% confidence limits = 0.27, 0.64) relative to inactive women. More recently, Rockhill et al found no relationship between strenuous exercise and breast cancer during 618,010 person years of follow-up in the Nurses Health Study II [4].

Factors that may reduce breast cancer risk in physically active women include: Delayed menarche (Early menarche is associated with increased breast cancer risk [5]. Delayed menarche is related to physical activity [2; 6]); Short luteal phase (Physically active women often have very short cycles with presumably short, inadequate luteal phases [7], oligomenorrhea and secondary amenorrhea [8].) Early menopause (Late menopause is reported to double the risk of breast cancer [9]. Earlier menopause has been reported for athletic, as compared to, non-athletic women [2].) Adiposity (Several studies report a positive association between upper body obesity and breast cancer [10; 11]. Athletic women have lower percent of body fat than non-athletic women.)

Whereas prior epidemiological studies on physical activity primarily focused on collegiate, occupational and leisure-time activities, the current study focuses on vigorous activity. Requiring continuous and sustained aerobic activity distinguishes running from occupational activity and many other sports. Our long-term objective is to test for a dose-response relation between distance run and breast cancer risk in 50,000 women runners. We will assess running level and other vigorous activities from questionnaires. This will be the first prospective study to concentrate on vigorous physical activity.

Body The purpose of the IDEA award is to establish a cohort of 50,000 who vigorously exercise, provide data on questionnaire validity and provide pilot data on surveillance. (Funding for surveillance will be deferred to a future funding application.) During this first year of funding we finalized the design of the survey questionnaire and obtained approval from human subjects for its use, determined the best recruit-

ment strategy for recruiting 50,000 women runners, obtained the names of over one-half million women runners, delivered the questionnaire to the printers for printing and collation, arranged for their mailing, and designed the system for archiving the surveys as they are received.

We have completed designing the initial survey questionnaire. Dr. Dee West, William Satariano, and Virginia Ernster reviewed the initial questionnaire and made a number of constructive comments. We revised and resubmitted the questionnaire to all three consultants who recommended further changes. All three consultants approved the final form of the questionnaire. After submission to human subjects, the final form received their approval on September 1, 1998.

We initially intended to include the survey in race packets distributed to runners by Runners' World magazine. Unacceptably low rates of return and high rates of cost per respondent (\$8.00) for these questionnaires precipitated a change in procedure. We therefore decided to obtain all of our questionnaires using direct mail solicitation. We purchased the names of 512,808 women runners from Runners' World magazine. This list includes the names of 378,147 women who participated in races during the last year, and 134,656 women who subscribe to Runner's World magazine. The questionnaires and mailing list are presently at the printers. Delivery is scheduled at the Berkeley City post office on October 23, 1998. The printers will deliver the questionnaires appropriately bundled for bulking mailing, including the survey and return envelope. Participant ID numbers will be stamped on each questionnaire upon returned.

We intended to create the cohort of 50,000 runners by adding 36,000 runners recruited through the current grant to our original cohort of 14,000 women runners collected between 1991 and 1996. Unfortunately, the consent for human subjects obtained for the initial 14,000 women runners is inconsistent with the Department of Defense human-use protocol. Rather than asking the earlier sample to re-consent, we will attempt to create a de novo sample of 50,000 women.

We have created a system to digitally archive the questionnaires as they arrive using TIFF files. We will use a KV-SS25 Document Scanner from Panasonic. This 20 ppm duplex document scanner provides a cost-effective approach to imaging forms with one-pass, double-sided scanning. The scanner supports scanning resolutions up to 300 dpi. and is equipped with an automatic document feeder (ADF) that holds up to 100 pages for unattended scanning.

We will use Alchemy software from IMR to organize the digitized questionnaires and to create self-contained, high performance databases on low-cost, recordable CDs. The software enables us to effectively browse, search and retrieve individual, hand-written questionnaires using a CD-ROM reader. The software provides highly compressed full-text indices, fast retrieval from large databases, profile field query, and high-performance document viewers.

The participant's name and address are printed directly on each questionnaire. Our software will read these data and the participant's ID number directly off the questionnaire using optical character recognition. This software will provide an archival

system to guarantee against accidental loss of data. Inclusion of the participant name and address in the database by scanning will reduce manual data entry cost. The system can store the names and addresses of the participant's contacts as images and print them directly as hand written address labels when required, also reducing data entry cost.

As stated in the outline of work, we are determining the feasibility of recontacting the runners. This is an ongoing effort. We have received questionnaires from 147 (56%) 264 runners initially contacted between 1991 and 1993. Two runners in this subsample did not respond due to death. We have subscribed to the DTEC and ID reports services supplied by the company Equifax. This service provides a current address based on a previous address or on the participant's social security number. Equifax has provided new addresses for 48% of the non-responders and confirmed the current addresses on 35%. Only 4% of the runners have unknown addresses.

Conclusion Thus in terms of the statement of work, we have created a survey questionnaire that represents the consensus of the principal investigator and consultants, we have identified a target population of over one-half million female runners, and we have established a system for archiving the questionnaires as they arrive. We anticipate recruiting 50,000 female runners by the end of January, 1999. We have launched our pilot study to determine the feasibility for follow-up and as of yet, have determined the vital status for 56% of the test cohort.

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National Runners' Health Study Questionnaire

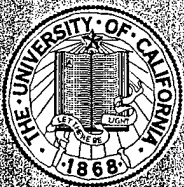
1. Birthdate (mo/day/yr): _____ / _____ / _____
 2. Sex (write number): 1) male 2) female.....
 3. Race (write number): 1) White 2) Hispanic 3) Black 4) Native-American 5) Asian/Pacific Is. 6) Other..
 4. Years of education (examples: HS = 12; B.S. or B.A. = 16; M.S. or M.A. = 18; Ph.D. or M.D. = 20)
 - 5-9. Average miles run each week for: 1994 _____ 1995 _____ 1996 _____ 1997 _____ 1998 _____
 10. During your usual run, how many minutes does it take for you to run one mile?
 11. At what age did you most recently start running 12 or more miles per week?
 12. What was your weight when you most recently started running 12 or more miles per week?
 13. What was your best 10-K time between 1994 and 1998 (leave blank if never run)?
 14. How many marathons did you run between 1994 and 1998 (write zero if none)?
 15. What was your best marathon time between 1994 and 1998?
 16. How many hours per week do you train for events that are 400 meters or less (write zero if none)?
 17. During an average week, how many miles is your longest run?
 18. During an average week, how many minutes do you spend stretching (write zero if none)?
 19. How many times per week do you run or do comparably vigorous exercise?
 20. During the last 3 months, how many days have you had to curtail your running due to injury?
 21. When you were in high school, how physically active were you compared with other students of the same gender? 1) less active; 2) average; 3) more active; 4) much more active
 22. What is your current height (in inches, without shoes)?
 23. What is your current weight (in pounds, pre-pregnancy weight if pregnant)?
 24. What is the most you have ever weighed (excluding pregnancies)?
 25. How old were you when you weighed the most?
 26. Do you have a twin (write number)? 0) no; 1) yes-fraternal; 2) yes-identical
 27. If you have ever had a heart attack, please give your age when it occurred (leave blank if never).
 28. Do you currently smoke cigarettes? 1) no-never smoked; 2) no-exsmoker; 3) yes-current smoker
 29. How many cigarettes per day were you smoking when you last smoked?
 30. How many total years had (have) you smoked (write zero if none)?
 31. If you are an exsmoker, how old were you when you quit (leave blank if not exsmoker)?
 32. During an average week, how many 4-oz. glasses of wine do you drink (write zero if none)?
 33. During an average week, how many 12-oz. bottles of beer do you drink (write zero if none)?
 34. During an average week, how many mixed drinks or liqueurs do you drink (write zero if none)?
 35. During an average week, how many milligrams (mg) of vitamin C supplement do you take (write zero if none)?
 36. During an average week, how many milligrams (mg) of vitamin E supplement do you take (write zero if none)?
 37. During an average week, how many milligrams (mg) of calcium supplement do you take (write zero if none)?
 38. During an average week, how many aspirin tablets do you take (write zero if none)?
 39. During an average week, how many servings of beef, lamb or pork do you eat (write zero if none)?
 40. During an average week, how many servings of fish do you eat (write zero if none)?
 41. During an average week, how many pieces of fruit do you eat (write zero if none)?
 42. Are you one of the following: 1) lactovegetarian; 2) strict vegetarian; 3) not vegetarian
 43. Women: a) At what age did you have your first menstrual period?
 - b) Do you currently have menstrual periods? 1) no; 2) yes; 3) not sure
 - c) If yes, how long is your usual cycle? (days from start of period to start of next period)
 - d) If you are no longer having menstrual periods, at what age did you stop?
 - e) How many total years have you used oral contraceptives (write zero if none)?
 - f) What age did you have your first full term pregnancy (leave blank if never)?
 - g) How many children have you had (write zero if none)?
 - h) How many total months have you breast fed (all pregnancies combined, write zero if never?
 - i) Has your uterus been removed? 1) no; 2) yes, removed; 3) unsure
 - j) Have your ovaries been removed? 1) no; 2) one removed; 3) both removed; 4) unsure
 44. Please provide, to the best of your ability, your body circumference in inches and bra cup:
- | | Now | At greatest weight | When started running | At 18 years old |
|------------------------|-------|--------------------|----------------------|-----------------|
| Chest (men and women): | _____ | _____ | _____ | _____ |
| Waist (men and women): | _____ | _____ | _____ | _____ |
| Hips (men and women): | _____ | _____ | _____ | _____ |
| Bra cup (women only): | _____ | _____ | _____ | _____ |

C.P.H.S.

98-2-76

EXPIRES

2/12/99



The National Runners' Health Study needs your help

By completing this questionnaire, you will be participating in an important research project which will test whether running prevents heart disease and breast cancer. **If you wish to take part in this important study, please complete the questionnaire, sign, and date below.** Send your research questionnaire to Paul Williams, Ph.D., Lawrence Berkeley National Laboratory, Bldg. 934, Berkeley, CA 94720. Our telephone number is (510) 486-5630. You must be at least 18 years old to participate. This research is funded in part by the United States government, including the National Institutes of Health and the Department of Defense.

45. Telephone: () _____
46. Birthdate (mo/day/yr): _____
47. Country of birth: _____
48. Social Security number: _____
(to identify deaths on National Death Index)
49. E-mail address: _____
50. Do you currently take medications? (write numbers)
0) none; 1) drugs for blood pressure; 2) drugs for thyroid; 3) drugs for cholesterol; 4) drugs for diabetes;
5) oral contraceptives; 6) estrogen only; 7) estrogen plus progesterone; 8) other female hormone replacement;
9) nonaspirin pain relief medication..... _____
Please provide product name and daily dose _____
51. If you, your biological parents, full siblings, or children ever had cancer, please provide the following:
a) relationship: _____; site: _____; age when diagnosed: _____
b) relationship: _____; site: _____; age when diagnosed: _____
c) relationship: _____; site: _____; age when diagnosed: _____
52. How many full brothers and sisters do you have? brothers: _____; sisters: _____
53. On average how many hours per week do you spend: running _____ cycling _____ swimming _____
other exercise (describe) _____
54. Please give us the names of 2 people who will know of your whereabouts for the next 10 years.
Name: _____
Address: _____
City, state, zip: _____
Telephone: () _____ () _____

55. Informed Consent: By signing below, I agree to the following: I understand that my participation in this research is completely voluntary and that I need not take part. I understand that I will be contacted at a future date in order to determine my health status and interest in related health studies, and that the researchers may find out whether I have had cancer or died through national health registries. I understand that nothing in this consent form is a waiver or release of my legal rights. I understand that the information provided to the National Runners' Health Study will be used for statistical purposes only and will remain confidential to the extent allowed by law. In the unlikely event of an investigation into the conduct of this research project the funding agencies may have access to my research record. I understand that I can stop participating in this study at any time, but that I cannot withdraw any information already submitted. I understand that if I suffer an injury as a direct and proximate result of participating in this study by filling out this survey or by supplying my medical information, medical care will be available to me. The cost of this care will be paid by the Regents of the University of California, pursuant to its contract with the United States Department of Energy. If you have any questions regarding this assurance, you may consult the Committee for Protection of Human Subjects, A & E Building, University of California, Berkeley CA 94720-1340; 510/642-7461.

Signature: _____ Date: _____

56. **(Very important but optional)** Permission to Release Medical Information: I hereby grant permission for the release of the following medical information to Paul Williams, Ph.D., who is conducting the National Runners Health Study: height, weight, cholesterol (total, HDL, LDL, VLDL), triglycerides, blood pressure, heart rate, uric acid, fasting glucose, and white blood-cell count.

Signature: _____ Date: _____

Name of primary care physician (print clearly): _____
Address: _____
City, state, zip: _____
Telephone (if known): _____